

BIF 2013 Emerging Technology Committee

**Update on genomic projects and
incorporation of marker information
into genetic analysis**

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Genomics

Ge no mics |jē'nōmiks, -'nām-, |
plural noun [treated as sing.]

the branch of molecular biology concerned with the structure, function, evolution, and mapping of genomes.

ORIGIN 1980s: from *genome* **'the complete set of genes present in an organism'** + *-ics*

NBCEC Mission

- Develop and implement improved predictions so selection can enhance economic viability of US beef cattle producers

www.nbcec.org

Genomic Prediction for National Cattle Evaluation Traits

- Operational
 - American Hereford Association
 - American Simmental Association
 - North American Limousin Foundation
 - Red Angus Association of America
- Near Operational
 - American Gelbvieh Association
 - Maine-Anjou Association of America
- Building Training Population
 - American Brangus Breeders Association
 - American International Charolais Association
- Note Canadian contributions from Genome Canada

"Current" 50k Sample Numbers

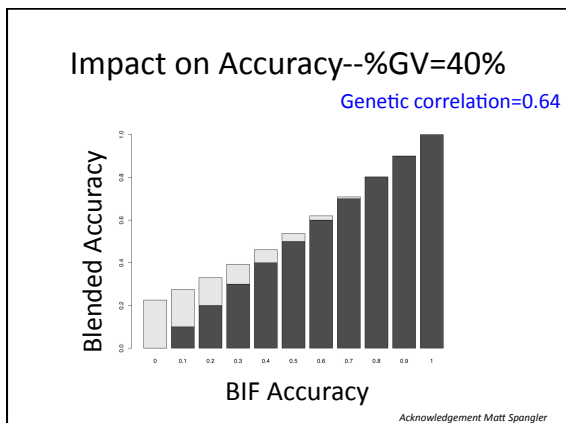
| | |
|--------|----------------------|
| 450 | BSH – Shorthorn |
| 5,557 | HER – Hereford |
| 1,794 | RAN – Red Angus |
| 5,240 | SIM – Simmental |
| 1,418 | BRG – Brangus |
| 11,334 | AAN – Aberdeen Angus |
| 3,275 | LIM – Limousin |
| 1,440 | GVH – Gelbvieh |
| 934 | CHA – Charolais |
| 948 | RDP – Maine Anjou |
| 32,392 | Total 50k Samples |

Excludes 700k, LD, GGP-LD, GGP-HD, *Bos indicus*

Change in AHA Predictive Accuracy

| Trait | Genetic Correlations | 2010 (800) | 2012 (1,081) | 2013 (2,980) |
|------------------|----------------------|------------|--------------|--------------|
| Birth weight | | 0.40 | 0.52 | 0.68 |
| Weaning wt | | 0.34 | 0.38 | 0.52 |
| Yearling wt | | 0.33 | 0.44 | 0.60 |
| Milk | | 0.21 | 0.26 | 0.37 |
| Calving Ease D | | | 0.42 | 0.68 |
| Calving Ease M | | | 0.20 | 0.51 |
| Fat | 0.43 | | 0.44 | 0.48 |
| Marbling | 0.29 | | 0.27 | 0.43 |
| Ribeye Area | 0.41 | | 0.45 | 0.49 |
| Scrotal Circum | 0.25 | | 0.27 | 0.43 |
| Mature Cow wt | | | | 0.64 |
| Average (% gVar) | | 0.33 (11%) | 0.37 (13%) | 0.52 (27%) |

Combined Pan-American International Evaluation Saatchi et al., JAS 2013; AAABG 2013



(50k) Predictive Abilities

| Trait | RedAngus (6,412) | Angus (3,500) | Hereford (2,980) | Simmental (2,800) | Limousin (2,400) | Gelbvieh (1,181) |
|----------|------------------|---------------|------------------|-------------------|------------------|------------------|
| BirthWt | 0.75 | 0.64 | 0.68 | 0.65 | 0.58 | 0.41 |
| WeanWt | 0.67 | 0.67 | 0.52 | 0.52 | 0.58 | 0.34 |
| YlgWt | 0.69 | 0.75 | 0.60 | 0.45 | 0.76 | |
| Milk | 0.51 | 0.51 | 0.37 | 0.34 | 0.46 | 0.34 |
| Fat | 0.90 | 0.70 | 0.48 | 0.29 | | |
| REA | 0.75 | 0.75 | 0.49 | 0.59 | 0.63 | 0.48 |
| Marbling | 0.85 | 0.80 | 0.43 | 0.63 | 0.65 | 0.56 |
| CED | 0.60 | 0.69 | 0.68 | 0.45 | 0.52 | 0.48 |
| CEM | 0.32 | 0.73 | 0.51 | 0.32 | 0.51 | |
| SC | | 0.71 | 0.43 | | 0.45 | 0.50 |

Genetic correlations from k-fold validation (training population size)
Saatchi et al (GSE, 2011; 2012; J Anim Sc, 2013)

Pooling Breeds

| Trait | Simmental from Single Breed | Simmental from Pooled Breeds |
|-------------------------|-----------------------------|------------------------------|
| Birth weight | 0.67 | 0.73 |
| Calving ease direct | 0.46 | 0.49 |
| Calving ease maternal | 0.31 | 0.29 |
| Carcass weight | 0.61 | 0.75 |
| Docility | 0.10 | 0.18 |
| Fat thickness | 0.19 | 0.26 |
| Marbling | 0.60 | 0.69 |
| Rib eye muscle area | 0.55 | 0.72 |
| Shear force | 0.52 | 0.60 |
| Stayability | 0.51 | 0.51 |
| Weaning weight direct | 0.56 | 0.63 |
| Weaning weight maternal | 0.32 | 0.28 |
| Yield grade | 0.73 | 0.91 |
| Yearling weight | 0.45 | 0.67 |

Pooling breeds does not typically hurt predictions (exception is for LIM)

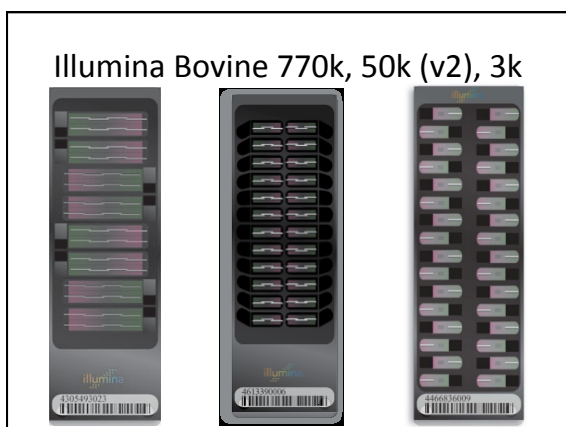
Saatchi & Garrick, WSASAS 2013

Prediction of Shorthorn only from other Breeds

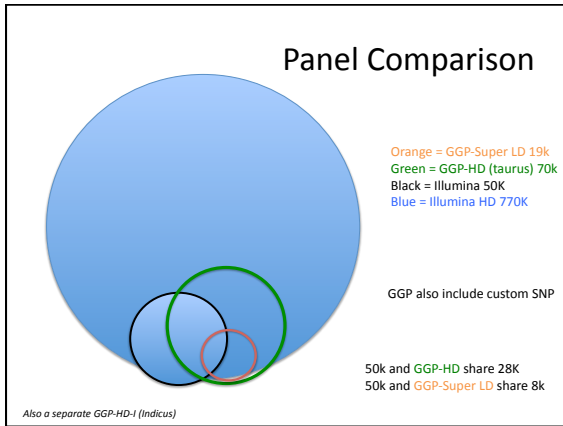
| | Angus | Brangus | Gelbvieh | Hereford | Limousin | Red Angus | Simmental |
|-----------------------|-------|---------|----------|----------|----------|-----------|-----------|
| Birth Weight | 0.08 | -0.05 | 0.09 | 0.23 | 0.18 | 0.40 | 0.37 |
| Calving ease direct | 0.05 | -0.01 | -0.16 | 0.17 | 0.15 | 0.23 | 0.30 |
| Calving ease maternal | 0.09 | 0.00 | | 0.08 | 0.15 | 0.06 | 0.07 |
| Carcass Weight | 0.20 | 0.05 | 0.07 | | -0.10 | 0.23 | 0.20 |
| Fat thickness | 0.17 | 0.02 | | 0.11 | | 0.08 | 0.01 |
| Milk | 0.09 | -0.04 | 0.16 | -0.06 | 0.02 | 0.03 | -0.06 |
| Marbling | 0.03 | -0.04 | 0.11 | -0.07 | -0.08 | 0.09 | 0.17 |
| Rib eye area | 0.03 | 0.01 | 0.12 | -0.07 | -0.01 | 0.05 | 0.08 |
| Weaning weight | 0.12 | -0.10 | 0.07 | 0.15 | -0.02 | 0.15 | 0.09 |
| Yearling weight | 0.09 | 0.00 | -0.08 | 0.14 | 0.02 | 0.13 | 0.13 |

Across breed prediction does not work if the breed is not in training

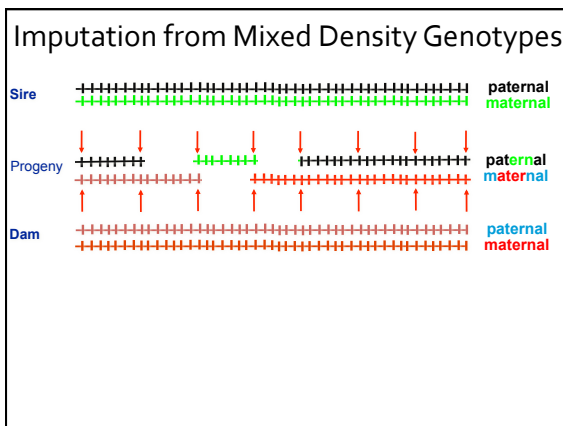
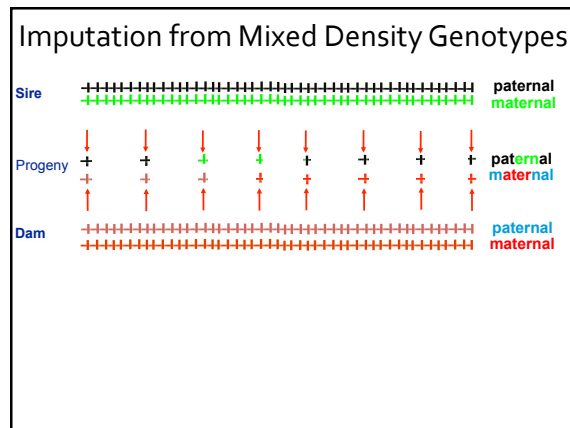
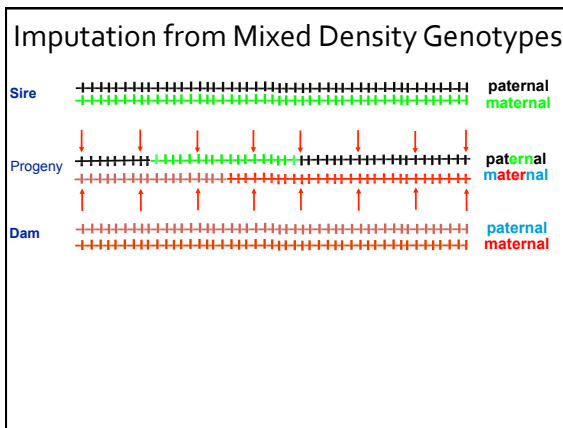
See also Kachman et al., 2013 GSE



- ### Different Illumina BeadChips
- Illumina
 - 50k \$80
 - Several versions
 - 700k (HD) \$185
 - 3k (LD) \$45
 - GeneSeek
 - GeneSeek Genomic Profilers
 - Low Density
 - Super GGP (20k) \$45
 - High Density
 - GGP HD (77k) \$75
 - GGP HD (Indicus)



- ### Imputation
- Is a method of determining some genotypes on a computer using actual genotypes on relatives
 - Provides options for cheaper routine genotyping
 - Requires relatives to have been genotyped at higher density
 - Will benefit from a larger training population
 - Will benefit from relatives having been genotyped
 - Requires knowledge of the order of markers



AHA Predictive Accuracy 2,980 6-fold

| Trait | Actual | Imputed |
|-------------------------|--------|---------|
| Birth Weight | 0.67 | 0.65 |
| Calving Ease Direct | 0.68 | 0.67 |
| Calving Ease Maternal | 0.51 | 0.50 |
| Fat Thickness | 0.47 | 0.46 |
| Marbling | 0.42 | 0.42 |
| Mature cow weight | 0.64 | 0.62 |
| Rib Eye Muscle Area | 0.49 | 0.46 |
| Serotal Circumference | 0.43 | 0.42 |
| Weaning Weight Direct | 0.53 | 0.50 |
| Weaning Weight Maternal | 0.37 | 0.35 |
| Yearling Weight | 0.61 | 0.59 |
| Mean | 0.53 | 0.51 |

Actual = 50k
Imputed = 10k

Major Regions for Birth Weight

Genetic Variance %

| Chr_mb | Angus | Hereford | Shorthorn | Limousin | Simmental | Gelbvieh |
|----------|-------|----------|-----------|----------|-----------|----------|
| 7_93 | 7.10 | 5.85 | 0.01 | 0.02 | 0.18 | 0.02 |
| 6_38-39 | 0.47 | 8.48 | 11.63 | 5.90 | 16.3 | 4.75 |
| 20_4 | 3.70 | 7.99 | 1.19 | 0.07 | 1.53 | 0.03 |
| 14_24-26 | 0.42 | 0.01 | 0.01 | 0.71 | 3.05 | 8.14 |

Some effects appear to be missing in some breeds
Some breeds may be nearly all homozygous
for the large or small variant on chromosomes 9 & 14?

Some of these same regions have big effects on one or more of
weaning weight, yearling weight, marbling, ribeye area, calving ease

QTL Characterization

AHA 2,980

| Genome | bw | ww | yw | mcw | ced |
|--------|-------|-------|-------|-------|------|
| bw | 1.00 | | | | |
| ww | 0.44 | 1.00 | | | |
| yw | 0.46 | 0.68 | 1.00 | | |
| mcw | 0.44 | 0.53 | 0.58 | 1.00 | |
| ced | -0.51 | -0.12 | -0.16 | -0.28 | 1.00 |
| Window | | | | | |
| 6_38 | 0.19 | 0.05 | 0.08 | 0.13 | 0.30 |
| 7_93 | 0.04 | 0.02 | 0.02 | 0.02 | 0.02 |
| 20_4 | 0.08 | 0.05 | 0.07 | 0.17 | 0.09 |

Genome shows genetic correlations, Window shows proportion genetic variance

Common haplotypes at BW QTL

20 SNP can have >1m haplotypes

Haplotypes from Beagle

| 7_93 (11 SNP) | 6_38 (23 SNP) | 20_4 (28 SNP) |
|------------------|-----------------------------|-------------------------------------|
| 1075 01101110111 | 216 10010000000111000010111 | 761 01001100110111000011010111111 |
| 253 00101110111 | 132 10111100010101011000110 | 136 0110100110110010011001101110111 |
| 181 11101110111 | 121 10011101011111010010101 | 124 01100101010000111010111100011 |
| 71 11101110101 | 118 10110100010111011010111 | 107 1110110011000000010010100011 |
| 58 01001110101 | 113 00110100011011000010111 | 88 11000110110010000101011111111 |
| 33 00100110101 | 95 10111100001101011000100 | 52 0110111110101111000011100001 |
| 29 01000110101 | 80 00011101111011010010101 | 50 0101110101111001010011111010 |
| 27 11001110101 | 74 1111110101010011101100 | 49 1111010011001110011011000001 |
| 24 11111110111 | 68 101111010101011000110 | 49 0100110110101110000010100010 |
| 22 11001110111 | 67 10010001000111000010111 | 31 0100110110001010001101011111 |
| 20 01100110111 | 63 11111100010110011101100 | 26 0110000101000000011011110011 |
| 19 00101110100 | 53 10111101011101011000100 | 22 0100100111001010001011000010 |
| 10 01101110100 | 52 1 1111101110010001111100 | 20 1100011011011000010101111111 |

Note there are no tag SNPs! Among 941 Herefords

7_93 (n>9) in Different Breeds

| | | | | | |
|-----|----------|----------|-----------|----------|---|
| 4/4 | 1655_AAN | 1655_HER | 1655_LIM | 1655_SIM | Some haplotypes shared across breeds |
| | 1789_AAN | 1789_HER | 1789_LIM | 1789_SIM | |
| | 1911_AAN | 1911_HER | 1911_LIM | 1911_SIM | |
| | 311_AAN | 311_HER | 311_LIM | 311_SIM | |
| 3/4 | 375_AAN | 375_HER | 375_LIM | 375_SIM | |
| | 887_AAN | 887_HER | 887_LIM | 887_SIM | |
| | 372_AAN | 372_HER | 372_LIM | 372_SIM | |
| | 1591_AAN | 1591_HER | 1591_LIM | 1591_SIM | |
| 2/4 | 1716_AAN | 1716_HER | 1716_LIM | 1716_SIM | Many private haplotypes so across breed prediction needs all breeds in training |
| | 1653_HER | 1653_LIM | 1653_SIM | | |
| | 1909_HER | 1909_LIM | 1909_SIM | | |
| | 823_HER | 823_LIM | 823_SIM | | |
| 1/4 | 116_AAN | 116_HER | 116_LIM | 116_SIM | |
| | 565_HER | 565_LIM | 565_SIM | | |
| | 629_HER | 629_LIM | 629_SIM | | |
| | 1652_LIM | 1652_SIM | | | |
| | 1844_LIM | 1844_SIM | | | |
| | 1845_LIM | 1845_SIM | | | |
| | 1847_LIM | 1847_SIM | | | |
| | 1908_LIM | 1908_SIM | | | |
| | 885_LIM | 885_SIM | | | |
| | 1_pteAAN | 2_pteHER | 11_pteLIM | 8_pteSIM | |

Segregation Status

- Determining the
 - frequency of the alternate QTL alleles
 - QTL genotype of individual animals

Multiple Trait Genomic Prediction

- Practically all genomic prediction analyses that allow SNP markers to have different weights, do this on a single trait basis
- We have prototyped an approach that allows multiple trait genomic prediction with different markers have different weights

Combined Analysis of Genotyped & Non-Genotyped Individuals

Henderson's Mixed Model Equations are the basis for National Cattle Evaluation

$$\begin{bmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{bmatrix} \begin{bmatrix} b \\ u \end{bmatrix} = \begin{bmatrix} X'R^{-1}y \\ Z'R^{-1}y \end{bmatrix}$$

Traditionally based on inverse relationship matrix

One approach to a "Single-step" analysis modifies the inverse of the pedigree-based relationship matrix according to a genomic relationship matrix H (below) is used in place of G (above)

$$H^{-1} = \left\{ \begin{matrix} A^{-1} + \begin{bmatrix} 0 & 0 \\ 0 & G^{-1} - A_{22}^{-1} \end{bmatrix} \end{matrix} \right\} \sigma_g^{-2}$$

Inverse pedigree relationship matrix Inverse genomic relationship matrix

Aguilar *et al.* (2010)

Summary

- Genomic prediction is an immature technology
 - Its accuracy exceeds parent average EPD
 - Accuracy is continuously improving
- Adoption is rapidly accelerating
- Currently used methodologies will soon be superseded with alternative approaches

Acknowledgements

| | | |
|---|--|--|
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